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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/538,106	03/29/2000	Frank McKeon	HMV-038.02	7239

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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 04/24/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/538,106

Applicant(s)

MCKEON F ET AL

Examiner

Christopher H Yaen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-10, 13 and 14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-10, 13 and 14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group III in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the rejection is not proper, because there is no burden placed on examiner upon examination. This is not found persuasive because group II and group III are drawn to methods using materially and patentably distinct products that are structural and functional different. The requirement is still deemed proper and is therefore made FINAL.

With regard to species election, because the species are from a non-elected claim, namely claim 1, the requirement for species election is withdrawn, and SEQ ID No. 1-12 will be rejoined. No species will be examined in this case, because they are all found in a non-elected claim. Claims 2-10 and 13-14 are examined on the merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

6 The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

OK 4. In regards to claims 2, 6, 10 and dependent claims thereof, in the recitation of the phrase "a decrease in the level of said p63", it is indefinite and unclear, because the amount of decrease needed to indicate malignant carcinoma is not known.

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5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 2-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the detection of malignant carcinomas, does not reasonably provide enablement for the diagnosis of carcinomas, detection of the onset of cancer, and distinguishing cervical squamous versus cervical small cell undifferentiated carcinoma. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instantly claimed invention provides methods for the diagnosis of carcinomas, detection of the onset of cancer, and distinguishing cervical squamous versus cervical small cell undifferentiated carcinoma. The specification provides description of detection methods of the p63 gene via methods such as immunohistochemical studies, but does not adequately describe in any detail how to diagnose, detect onset and distinguish samples that are cancerous versus non cancerous. There is a lack of an enabling disclosure especially for how much of a decrease over normal tissues samples that would be an indication of a cancerous phenotype. Because the specification is silent in this regard, it would force the skilled artisan into undue experimentation.

The factors which must be considered in determining undue experimentation are set forth in In re Wands 8 USPQ2d 1400. The factors include: (1) quantity of

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experimentation, (2) the amount of guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the predictability of the art, and (7) breadth of the claims.

With regard to factors one and two cited above the quantity of experimentation needed to determine what levels of p63 protein is normal versus what levels are considered low leading to a cancerous phenotype, would require experimentation. The instantly disclosed specification only provides the initial experimentation that is needed to determine such levels, in this regard, there is an inadequate amount of guidance to practice the instantly claimed invention.

With regard to factors four, five, and six cited above, it is noted that there is a great deal of unpredictability and inaccuracy associated with the diagnosis of cancer using protein levels as indicated by Righi E *et al.* (Diagn Cytopathol 1997 Dec; 17(6):436-9 see abstract). The instant specification fails to provide specific methodological procedures or steps for which the instant method can be used to diagnose cancer.

With regard to factor three and seven cited above, it is noted that the working examples are limited to the detection of p63 gene by immunohistochemical methods. Although immunohistochemical methods are qualitative, it is hard to provide any quantitative measurements that would provide an accurate indication of a decrease of any protein levels. Such is not seen as sufficient to support the breadth of the claims, wherein the scope of the claims encompasses diagnosis of cancer. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to

use applicant's alleged discovery, not how to find out how to use it for themselves., see In re Gardner et al. 166 USPQ 138 (CCPA 1970).

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 6-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Hall *et al.* (Carcinogenesis 2000 Feb; 21(2):153-60). Claims 6-9 are drawn to methods of detecting the onset of cancer in sub-columnar reserve cells (cervical, breast, prostate, kidney, testis, adrenal gland, brain, spleen, and thymus), by determining the level of p63 gene product (protein). Hall *et al.* disclose of the detection of p63 protein by immunohistochemical and immunoblot methods in breast, spleen, and kidney (pg 155 fig 3 and pg 156 fig 4). Furthermore, Hall *et al.* also disclose that p63 ($\Delta Np63\alpha$) is also found in neoplastic tissues. Therefore, the invention as claimed is anticipated.

9. Claims 13 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Hall *et al.* (Carcinogenesis 2000 Feb; 21(2):153-60). Claims 13 and 14 are drawn to a kit for diagnosing malignant carcinoma comprising p63 antibody. Hall *et al.* disclose of an antibody that is reactive to $\Delta Np63\alpha$. Therefore, the invention as claimed is anticipated.

Claim Rejections - 35 USC § 103

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10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 2-6, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hall *et al.* (Carcinogenesis 2000 Feb; 21(2):153-60) in view of Parsa R *et al.* (J. Invest Dermatol 1999 Dec; 113(6):1099-1105).

Claims 2-6, and 10 are drawn to methods of diagnosing malignant carcinomas (claims 2-6) and distinguishing cervical squamous carcinomas from cervical small cell undifferentiated carcinoma (claim 10) by determining the level of p63 gene product (protein).

13. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Hall *et al.* disclose of detecting p63 protein by using immunohistochemical and immunoblot techniques. In addition, Hall *et al.* also disclose that the tissue types that are involved are breast, kidney, and spleen (see fig 3 pg155). Hall *et al.* do not disclose the detection of p63 in squamous cell carcinomas. Parsa R *et al.*, however, do disclose of detection of p63 in squamous cell carcinomas (see abstract). Both references disclose of p63's homology to p53, a known cancer marker.

It would have been obvious to one of skill in the art at the time the invention was made to diagnose and distinguish carcinomas by determining p63, because the prior art provides sufficient motivation to practice the invention as claimed. The suggestion/motivation for doing what the applicant has claimed is that it was known in the art at the time the invention was made, that p63 was known to be associated with cancer as disclosed in both Hall *et al.* and Parsa *et al.* Also, it was already known that detection methods for p63 were available and that p63 as disclosed in both Hall *et al.* and Parsa *et al.* were closely related to p53, a cancer marker already in use for the detection of cancer. Furthermore, Parsa *et al.* disclosed of a method for the detection of squamous cell carcinomas.

Therefore, it would have been *prima facie* obvious at the time the invention was made, that one of ordinary skill in the art would be able to derive a method of diagnosing and/or distinguishing carcinomas. The art at the time the invention was

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made provided all the motivation needed to accomplish the claimed invention, because p53 a known marker for cancer was already highly studies in the art as a potential/efficient marker for cancer. It was also known that p53 and p63 were closely related as disclosed in both Hall *et al.* and Parsa *et al.* Due to the close relation of the two proteins, it would have been obvious to use p63 as a diagnostic marker for cancer. In addition, Hall *et al.* already disclosed a method of detecting p63, and suggested that this protein can be used to distinguish between normal epithelial tissues and malignant tissues, hence carcinomas. Parsa *et al.*'s disclosure of the detection of squamous cell carcinomas would help lead one of skill in the art to determine that there could be a distinguishable feature from small cell undifferentiated carcinoma.

Conclusion

14. No claims allowed

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

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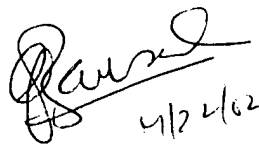
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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen

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April 15, 2002

Handwritten signature of Geetha P. Bansal in cursive script.

GEETHA P. BANSAL
PRIMARY EXAMINER